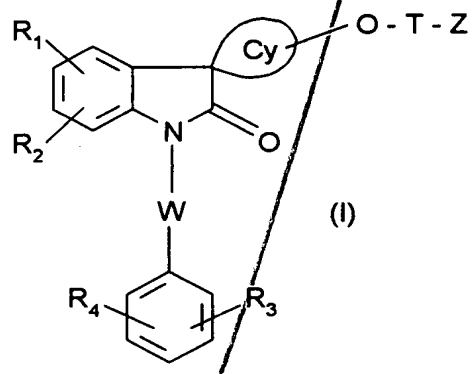
CLAIMS

1. Compound of formula



(I)

in which:

- R_1 and R_2 each independently represent a hydrogen; a hydroxyl; a halogen; a (C_1-C_7)alkyl; a (C_1-C_7)polyfluoroalkyl; a (C_1-C_7)alkoxy; a (C_1-C_7)-alkylthio; a (C_1-C_7)polyfluoroalkoxy; a (C_3-C_7)cycloalkyloxy; a (C_3-C_7)cycloalkylthio; a cycloalkylmethoxy or a cycloalkylmethylthio in which the cycloalkyl is C_3-C_7; a phenoxy; a benzyloxy; a nitro; or a cyano;

- R_3 and R_4, independently of one another, substitute the phenyl group one or a number of times and each independently represent a hydrogen; a halogen; a (C_1-C_7)alkyl; a (C_2-C_7)alkenyl; a (C_1-C_7)polyhaloalkyl; a phenyl or a benzyl; a cyano; a nitro; an $-NR_5R_6$ group; a hydroxyamino; a hydroxyl; an OR_7 group; an SR_7 group; a $-COOR_8$ group, a $-CONR_9R_{10}$ group; or a $-CSNR_9R_{10}$ group, at least one of the R_3 and R_4 radicals being other than hydrogen;

- R_5 and R_6 each independently represent a hydrogen; a (C_1-C_7)alkyl; a (C_2-C_7)alkenyl; a phenyl; a benzyl; a (C_1-C_7)alkylcarbonyl; a (C_1-C_7)thiocarbonyl; a (C_3-C_7)cycloalkylcarbonyl; a (C_3-C_7)cycloalkylthiocarbonyl; a benzoyl; a thienylcarbonyl; a furylcarbonyl; a (C_1-C_7)alkyloxycarbonyl; a phenoxycarbonyl; a benzyloxycarbonyl; a carbamoyl or a thiocarbamoyl which is unsubstituted or substituted by R_9 and R_{10} or

Replaced by Article 34

alternatively R_5 and R_6 form, with the nitrogen atom to which they are bonded, a heterocyclic group chosen from the pyrrolidine, pyrroline, pyrrole, indoline, indole and piperidine groups;

- R_7 represents a (C_1-C_7)alkyl; a (C_2-C_7)alkenyl; a phenyl; a benzyl; a (C_3-C_7)cycloalkyl; a (C_1-C_7)polyfluoroalkyl; a formyl; a (C_1-C_7)alkylcarbonyl; a benzoyl; or a benzylcarbonyl;

- R_8 represents a hydrogen; a (C_1-C_7)alkyl; a phenyl; or a benzyl;

- R_9 and R_{10} each independently represent hydrogen; a (C_1-C_7)alkyl; a (C_1-C_7)polyfluoroalkyl; a (C_2-C_7)alkenyl; a (C_3-C_7)cycloalkyl optionally substituted by a hydroxy (C_1-C_4)alkyl; a pyridyl; a phenyl; a thienyl; a furyl; or alternatively R_9 and R_{10} form, with the nitrogen atom to which they are bonded, a heterocyclic group chosen from the pyrrolidine, piperidine or piperazine groups, which is unsubstituted or substituted by (C_1-C_4)alkyls; or a (C_4-C_7)azacycloalkyl;

- W represents a $-CH_2-$ or $-SO_2-$ group;

- Cy forms, with the carbon to which it is bonded, a non-aromatic, saturated or unsaturated C_3-C_{12} hydrocarbon ring which is optionally condensed or substituted by one or a number of (C_1-C_7)alkyl groups, it being possible for the said groups to substitute the same carbon atom one or a number of times, or by a C_3-C_6 spirocycloalkyl;

- T represents a (C_1-C_4)alkylene which is optionally interrupted by a (C_3-C_6)cycloalkylene, the said alkylenes optionally being substituted one or a number of times on the same carbon atom by a (C_1-C_3)alkyl; or alternatively T represents a direct bond;

- Z represents an $-NR_{11}R_{12}$ group; $-^{+}NR_{11}R_{12}(C_1-C_4)$-alkyl (A^-), (A^-) being an anion, preferably Cl^-, Br^-, I^- or $CH_3SO_4^-$; $-N(O)R_{11}R_{12}$; a $-COOR_{11}$ group; an $-NR_{11}COR_{12}$ group; a (C_1-C_4)alkyloxycarbonylamino; a benzyloxycarbonylamino; a $-CONR_{11}R_{12}$ group; it being understood

that when T represents a methylene or a direct bond, Z cannot be $-NR_{11}R_{12}$; $-^{+}NR_{11}R_{12}(C_1-C_4)$alkyl; $-N(O)R_{11}R_{12}$; $-NR_{11}COR_{12}$; a (C_1-C_4)alkyloxycarbonylamino; a benzyloxycarbonylamino;

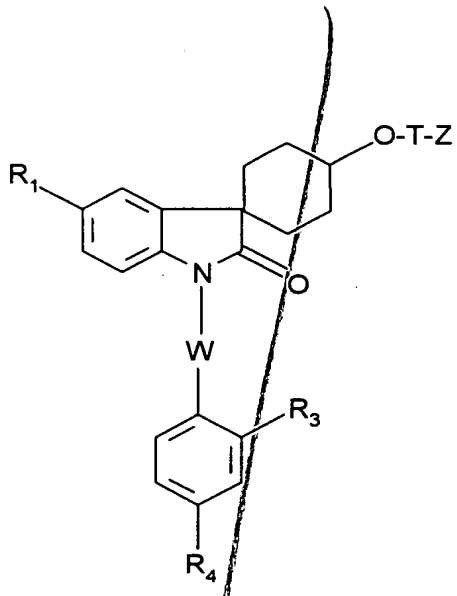
- R_{11} and R_{12} each independently represent hydrogen; a (C_1-C_7)alkyl; a (C_1-C_4)alkoxy; a (C_3-C_7)cycloalkyl; a phenyl; a (C_1-C_3)alkylenecycloalkyl, in which the cycloalkyl is C_3-C_7, or a (C_1-C_3)alkylenephenyl, it being possible for the said groups optionally to be mono- or polysubstituted by R_{13} ;

or alternatively R_{11} and R_{12} optionally form, with the nitrogen atom to which they are bonded, a heterocycle chosen from azetidine, pyrrolidine, piperidine, piperazine, piperazinone, morpholine, morpholinone, thiomorpholine and hexahydroazepine heterocycles, which heterocycle is optionally mono- or polysubstituted by R_{13}; or a thiomorpholine 1,1-dioxide or a thiomorpholine 1-oxide; or alternatively R_{12} represents a pyrrolidone or a piperidone ;

- R_{13} represents a hydroxyl group; a (C_1-C_4)alkyl; a (C_1-C_4)alkoxy; a thiol; a (C_1-C_4)alkylthio; a (C_1-C_4)-alkylsulphinyl; a (C_1-C_4)alkylsulphonyl; a benzyloxy; a hydroxyalkyloxy; an $-NR_{14}R_{15}$ group in which R_{14} and R_{15} each independently represent hydrogen or a (C_1-C_4)alkyl or a (C_1-C_4)alkyloxycarbonyl or a benzyloxycarbonyl; a carboxyl; a (C_1-C_4)alkyloxycarbonyl, a phenoxycarbonyl, a benzyloxycarbonyl ; a carbamoyl; an amidino; a guanidino; an imidazolyl; a thienyl; a pyridyl; an indolyl; or a tetrahydroisoquinolyl;

and their salts.

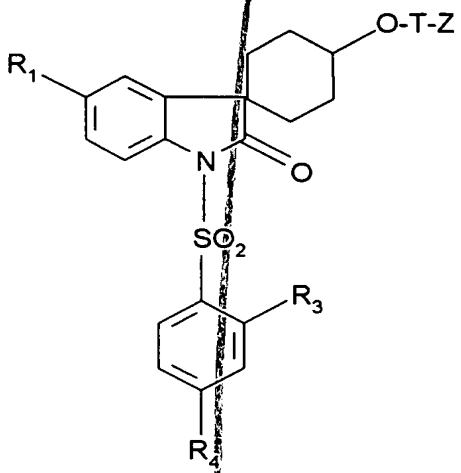
2. Compound of formula:



(I.1)

in which R_1, R_3, R_4, W, T and Z are as defined for (I) or one of their salts, solvates or hydrates.

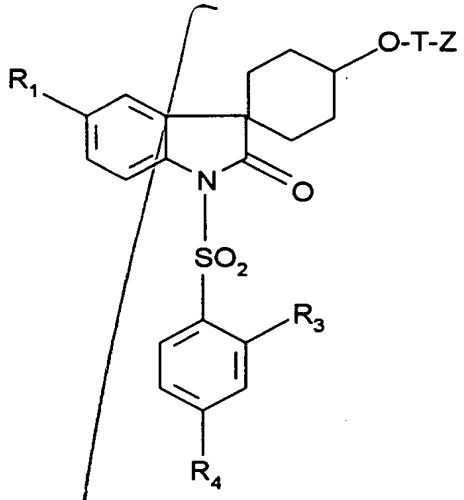
3. Compound of formula:



(I.2)

in which R_1, R_3, R_4, T and Z are as defined for (I) or one of their salts, solvates or hydrates.

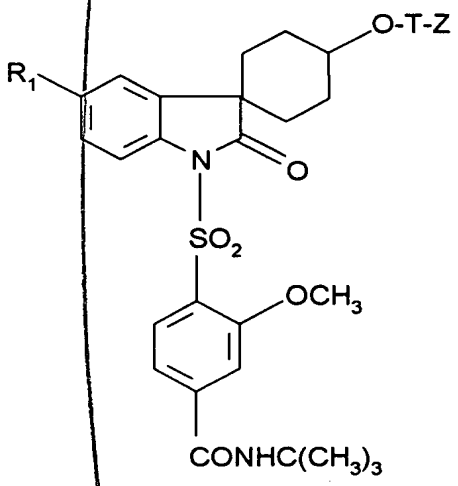
4. Compound of formula:



(I.3)

in which R_1, R_3 and R_4 are as defined for (I), T represents a (C_1-C_3)alkylene and Z represents an amino group, a 2-hydroxyethylamino, a 2-(2-hydroxy)ethyloxy-ethylamino, a morpholinyl or a carboxylic acid, and its salts, solvates or hydrates.

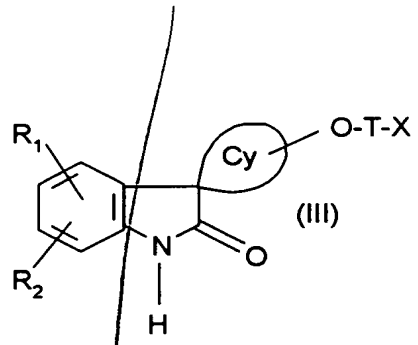
5. Compound of formula:



(I.4)

in which R_1, T and Z are as defined for (I) or one of its salts, solvates or hydrates.

6. Compound of formula:



in which R_1, R_2, Cy, T and X are as defined for (I)

- X is a nucleofuge group such as a halogen, preferably bromine, chlorine or iodine, or a sulphonic acid derivative, such as tosyloxy, mesyloxy;

- or alternatively X represents a reducible group, such as an azide,

or one of its salts, solvates or hydrates.

7. Compound of formula:

*5-chloro-3-spiro-[4-(2-morpholinoethyloxy)cyclohexane]-1-[4-(N-*tert*-butylcarbamoyl)-2-methoxybenzenesulphonyl]indolin-2-one;

*5-ethoxy-3-spiro-[4-(2-aminoethyloxy)cyclohexane]-1-[4-(4-N-*tert*-butylcarbamoyl)-2-methoxybenzenesulphonyl]indolin-2-one;

*5-ethoxy-3-spiro-[4-(2-(N-methyl-N-(2-hydroxyethyl)amino)ethyl)oxycyclohexane]-1-[4-(N-*tert*-butylcarbamoyl)-2-methoxybenzenesulphonyl]indolin-2-one;

*5-ethoxy-3-spiro-[4-(2-morpholinoethyloxy)cyclohexane]-1-[4-(N-*tert*-butylcarbamoyl)-2-methoxybenzyl]-indolin-2-one;

*5-ethoxy-1-[4-(N-*tert*-butylcarbamoyl)-2-methoxybenzenesulphonyl]-3-spiro-[4-(2-morpholinoethyloxy)-cyclohexane]indolin-2-one;

*5-ethoxy-3-spiro-(4-carboxymethyloxycyclohexane)-1-(4-N-*tert*-butylcarbamoyl-2-methoxybenzenesulphonyl)-indolin-2-one;

*5-ethoxy-3-spiro-[4-(2-morpholinoethyloxy)cyclohexane]-1-[4-(N-*tert*-amylbutylcarbamoyl)-2-methoxybenzenesulphonyl]indolin-2-one;

*5-ethoxy-3-spiro-[4-(2-carboxyethyloxy)cyclohexane]-1-[4-(N-*tert*-amylcarbamoyl)-2-methoxybenzenesulphonyl]indolin-2-one;

*5-ethoxy-1-[4-(N',N'-diethylureido)-2-methoxybenzenesulphonyl]-3-spiro-[4-(2-dimethylaminoethyloxy)-cyclohexane]indolin-2-one;

*5-Ethoxy-3-spiro-[4-(2-(4-ethoxypiperidino)-ethyloxy)cyclohexane]-1-[4-(N-*tert*-butylcarbamoyl)-2-methoxybenzenesulfonyl]indolin-2-one ;

*5-Ethoxy-3-spiro-[4-(2-glycylaminoethyloxy)-cyclohexane]-1-[4-(N-*tert*-butylcarbamoyl)-2-methoxybenzenesulfonyl]indolin-2-one ;

*5-Ethoxy-3-spiro-[4-(2-(N,N-dimethylglycylamino)-ethyloxy)cyclohexane]-1-[4-(N-*tert*-butylcarbamoyl)-2-methoxybenzenesulfonyl]indolin-2-one ;

*5-Chloro-3-spiro-[4-(N-(3-dimethylaminopropyl)-carbamoylmethyloxy)cyclohexane]-1-[4-(N-*tert*-butylcarbamoyl)-2-methoxybenzenesulfonyl]indolin-2-one ;

*5-Ethoxy-3-spiro-[4-(2-(4-dimethylaminobutyryl-amino)ethyloxy)cyclohexane]-1-[4-(N-*tert*-butylcarbamoyl)-2-methoxybenzenesulfonyl]indolin-2-one ;

*5-Ethoxy-3-spiro-[4-(2-(2-hydroxyethylamino)-ethyloxy)cyclohexane]-1-[4-(N-*tert*-butylcarbamoyl)-2-methoxybenzenesulfonyl]indolin-2-one ;

*5-Ethoxy-3-spiro-[4-(2-(-L-γ-glutamylamino)-ethyloxy)cyclohexane]-1-[4-(N-*tert*-butylcarbamoyl)-2-methoxybenzenesulfonyl]indolin-2-one ;

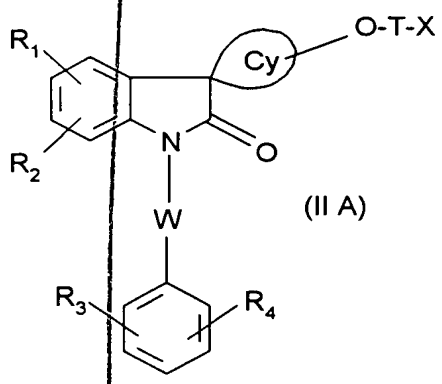
*5-Ethoxy-3-spiro-[4-(2-(-L-pyroglutamylamino)-ethyloxy)cyclohexane]-1-[4-(N-*tert*-butylcarbamoyl)-2-methoxybenzenesulfonyl]indolin-2-one ;

*5-Ethoxy-3-spiro-[4-(2-(2-(2-hydroxyethyloxy)-ethylamino)ethyloxy)cyclohexane]-1-[4-(N-*tert*-butylcarbamoyl)-2-methoxybenzenesulfonyl]indolin-2-one ;

and their pharmaceutically acceptable salts, solvates or hydrates being particularly suited to use in pharmaceutical formulations.

8. Process for the preparation of a compound of formula (I) according to any one of Claims 1 to 4, characterized in that:

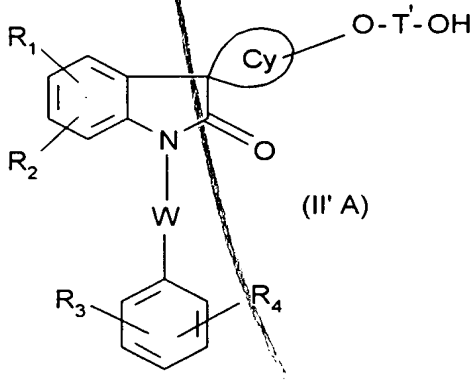
(1) either a compound of formula:



(II A)

in which R_1, R_2, R_3, R_4, W, Cy and T are as defined for (I) and in which X is a nucleofuge group, such as a halogen, preferably bromine, chlorine or iodine, or a sulphonic acid derivative, such as tosyloxy or mesyloxy, is reacted with a derivative of formula ZH (1) in which Z is as defined for (I) containing a nucleophilic group capable of displacing X, for example a primary or secondary amine, preferably a secondary amine, in polar solvents, such as dimethylformamide, tetrahydrofuran or acetonitrile, at temperatures of between 0° and 120°C, or alternatively X represents a reducible group, such as an azide, which is subsequently reduced to amino;

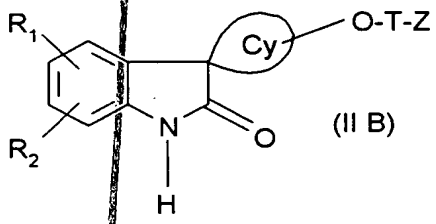
(2) or, when Z = -COOH, a compound of formula:



(II' A)

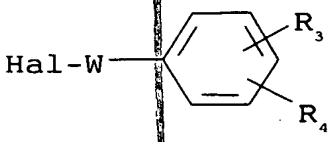
in which R_1, R_2, W, R_3, R_4 and Cy are as defined for (I) and T' represents T-CH_2-, is reacted with an oxidizing agent, such as chromium oxide in an acid solvent, such as dilute acetic acid at a temperature of between 0°C and 100°C, alkali metal dichromates or alkali metal or alkaline-earth metal permanganates;

(3) or a compound of formula:



(II B)

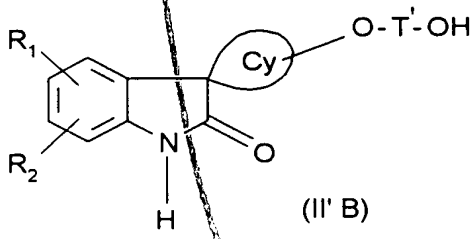
in which R_1, R_2, Cy, T and Z are as defined for (I), is reacted with a compound of formula:



(2)

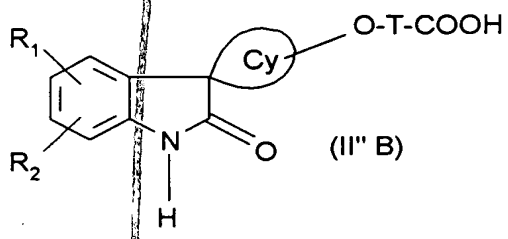
in which W, R_3 and R_4 are as defined for (I) and Hal represents a halogen atom, in an anhydrous solvent, such as dimethylformamide or tetrahydrofuran, in the presence of a metal hydride, such as, for example, sodium hydride, or an alkali metal alkoxide, such as, for example, potassium *tert*-butoxide, at temperatures of between -40° and 25°C;

(4) or, when Z = -COOH, a compound of formula:



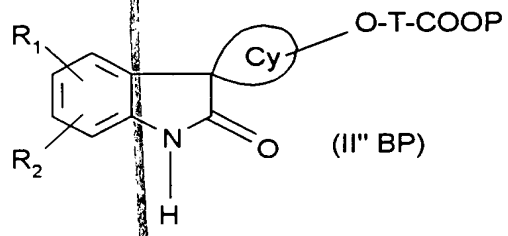
(II' B)

in which R_1, R_2 and Cy are as defined above for (I) and T represents T-CH_2, is reacted with an oxidizing agent described above for the conversion of (II'A) to (I), then the acid thus obtained of formula:



(II" B)

in which R_1, R_2, Cy and T are as defined above for (I), is subsequently optionally protected by a protective group for the carboxylic acid, in order to obtain the intermediate of formula:



(II" BP)

in which R_1, R_2, Cy and T are as defined for (I) and P represents a protective group chosen from an alkyl, a *tert*-butyl or a benzyl, and, finally, this compound (II"BP) is subjected to the action of a derivative of formula (2) in order to obtain, after deprotection, a compound (I); one of its quaternary ammoniums, oxides, sulphones or salts.

9. Pharmaceutical composition containing, as active principle, a compound of formula (I) according to Claim 1 or one of its pharmaceutically acceptable salts, hydrates or solvates.

10. Pharmaceutical composition containing, as active principle, a compound of formula (I.1) according to Claim 2 or one of its pharmaceutically acceptable salts, hydrates or solvates.

11. Pharmaceutical composition containing, as active principle, a compound of formula (I.2) according to Claim 3 or one of its pharmaceutically acceptable salts, hydrates or solvates.

12. Pharmaceutical composition containing, as active principle, a compound of formula (I.3) according to Claim 4 or one of its pharmaceutically acceptable salts, hydrates or solvates.

13. Pharmaceutical composition containing, as active principle, a compound of formula (I.4) according to Claim 5 or one of its pharmaceutically acceptable salts, hydrates or solvates.

14. Pharmaceutical composition containing, as active principle, a compound according to Claim 7.

15. Pharmaceutical composition according to any one of Claims 9 to 14 also containing another active principle.

16. Pharmaceutical composition according to Claim 15, characterized in that the other active principle is a specific antagonist of the angiotensin II receptor.

17. Pharmaceutical composition according to Claim 16, characterized in that the specific antagonist of the angiotensin II receptor is irbesartan.

18. Pharmaceutical composition containing a combination of 5-ethoxy-1-[4-(N-*tert*-butylcarbamoyl)-2-methoxybenzene-sulphonyl]-3-spiro-[4-(2-morpholinoethyloxy)cyclohexane]-indolin-2-one and irbesartan.